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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/663,020	09/15/2000	Jeffery W. Bacher	16026-9267	1823

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EXAMINER
CHUNDURU, SURYAPRABHA

ART UNIT	PAPER NUMBER
1656	9

DATE MAILED: 11/27/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/663,020	Applicant(s) BACHER ET AL.	
	Examiner Suryaprabha Chunduru	Art Unit 1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 August 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-47* is/are pending in the application.

4a) Of the above claim(s) *3,17 and 35-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-16 and 18-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. The Information Disclosure Statement (Paper No. 3) filed on December 18, 2000 has been entered.

2. The response to restriction requirement (Paper No. 7) filed on August 29, 2001 has been entered.

3. Applicant's election with traverse of claims in Group I in Paper No. 7 is acknowledged. The traversal is on the ground(s) that the Group I and II are related. This is not found persuasive because claims are grouped based on broadest claims as claim 1 and intended use of kit claims has no patentable weight. M.P.E.P. 2111.01 states that "any terminology in the preamble that limits the structure of the claimed invention must be treated as a claim limitation. See, e.g., Corning Glass Works v. Sumitomo Elec. U.S.A.,Inc., 868 F.2d 1251, 1257, 9 USPQ2d 1962, 1966 (Fed. Cir. 1989) (The determination of whether preamble recitations are structural limitations can be resolved only on review of the entirety of the application "to gain an understanding of what the inventors actually invented and intended to encompass by the claim."); Pac-Tec Inc. v. Amerace Corp.,903 F.2d 796, 801, 14 USPQ2d 1871, 1876 (Fed. Cir. 1990) (determining that preamble language that constitutes a structural limitation is actually part of the claimed invention). See also In re Stencel, 828 F.2d 751, 4 USPQ2d 1071 (Fed. Cir. 1987). The claim preamble must be read in the context of the entire claim. The determination of whether preamble recitations are structural limitations or mere statements of purpose or use"can be resolved only on review of the entirety of the [record] to gain an understanding of what the inventors actually invented and intended to encompass by the claim." Corning Glass Works, 868 F.2d at 1257, 9 USPQ2d at 1966".

Applicants' argue that the primers in method claims are required by claimed kits which not found persuasive because the kits could be used in simple hybridization assays, or the primers could be used in cloning or applied to affinity columns as in purification assays. Further, additional search is required to review not only the patents in class 435, subclass 6 for Group I but also the patents in class 536, subclass 22.1 for Group II. Review of these additional searches is prima facie evidence of burden, which is not rebuted. The requirement is still deemed proper and is therefore made FINAL.

4. Claims 3 and 17 are dependent on non-elected species and therefore are not considered for examination. Claims 1-2, 4-16, and 18-34 are considered for examination with respect to MONO-15 species (SEQ ID No. 7 and 8). Non-elected Group II Claims 35-47 are withdrawn from further consideration.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11-13 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01.

Method claims require a last step or phrase in the last step that states the accomplishment of the goals for the method which were stated in the method's preamble. Claims 11-13 lack such a last step (how cancerous tumors are prognosed or diagnosed or detected) and are confusing because the additional method step is not sufficiently set forth. While minute details are not required in method claims, at least the basic steps must be recited in a positive, active fashion.

See Ex parte Erlich, 3 USPQ2d1011, p.1011 (Bd. Pat. App. Int. 1986). It is suggested that amended claims more clearly describing the intended steps be submitted.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

a. Claims 1-2, 9-16, 21, 24-28 and 31-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ruschoff et al. (USPN. 6,150,100) and in view of Schumm et al. (5,843,660).

Ruschoff et al. teach a method for genomic instability (micro-satellite instability) at selected micro-satellite loci wherein Ruschoff et al. disclose that the method comprises (i) isolating DNA from human biological material, providing primers for each set of micro-satellite loci comprising mononucleotide repeat locus, dinucleotide repeat loci, tetranucleotide repeat loci, pentanucleotide loci (see column 6, lines 33-43) amplifying the set of micro-satellite loci of

sample DNA and determining the size of amplified DNA fragments (see column 3, lines 7-18). Ruschoff et al. also disclose that (i) the method comprises amplification of genomic DNA from normal tissue (non-cancerous) and genomic DNA from tumor tissue (see column 30, lines 43-59); the biological material includes DNA isolated from tumor tissue, body fluids such as blood, serum, plasma, urine or faeces (see column 4, lines 17-25); (iii) the method is applicable to prognostic diagnosis of tumors and analysis of these loci was suitable (used) for making prognostic tumor diagnosis, tumor predisposition as well as detection of tumors of endometrium, the gastrointestinal tract and in particular colorectal tumors (see column 3, lines 42-45). However, Ruschoff et al. did not teach multiplex amplification.

Schumm et al teach a multiplex amplification method to amplify short tandem repeat loci wherein Schumm et al. disclose that the method comprises co-amplification of at least three tandem repeat loci from one or more DNA samples and evaluating the amplified alleles in the mixture by comparing amplified alleles to a size standard (see column 4, lines 11-27 and column 6, lines 29-33). Further, Schumm et al. disclose that the method allows three or more, even as many as eight or more loci to be amplified in one tube using a single amplification reaction (see column 7, lines 61-67) and use of primers either labeled or unlabelled to evaluate the amplified alleles (see column 7, lines 36-60).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the method of analyzing micro-satellite instability as taught by Ruschoff et al. with the method of multiplex amplification as taught by Schumm et al., because Ruschoff et al. states that 'it was determined that in different patients different classes of micro-satellites are affected with different frequencies of genomic instability, consequently an

analysis of different classes of micro-satellite instability(MIN) is essential for a reliable determination of the RER phenotype with a limited number of PCR reactions' (see column 3, lines 1-5). One such alternative form of analysis to limit the PCR reactions expressly motivated by Schumm et al. is the use of multiplex amplification with different samples and multiple loci specific primers in one tube PCR reaction 'to provide a method for simultaneous amplification of multiple distinct polymorphic short tandem repeat loci using PCR or other amplification systems to determine, in one reaction, the alleles of each locus contained within the multiplex' (see column 3, lines 54-59). An ordinary practitioner would have been motivated to combine the method of Ruschoff et al. with the method of Schumm et al. in order to achieve the expected advantage of a rapid and sensitive method for detecting microsatellite instability.

b. Claims 4-8,18-20, 22-23, and 29-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ruschoff et al. (USPN. 6,150,100) and in view of Schumm et al. (5,843,660). Further in view of Kieback (USPN. 5,645,995) and Sulston et al. (Genome Res., 8(11), 1097-1108, 1998, Sequence alignment from GenEmbl database).

Ruschoff et al. teach a method for genomic instability (micro-satellite instability) at selected micro-satellite loci wherein Ruschoff et al. disclose that the method comprises (i) isolating DNA from human biological material, providing primers for each set of micro-satellite loci comprising mononucleotide repeat locus, dinucleotide repeat loci, tetranucleotide repeat loci, pentanucleotide loci (see column 6, lines 33-43) amplifying the set of micro-satellite loci of sample DNA and determining the size of amplified DNA fragments (see column 3, lines 7-18). Ruschoff et al. also disclose that (i) the method comprises amplification of genomic DNA from normal tissue (non-cancerous) and genomic DNA from tumor tissue (see column 30, lines 43-

59); the biological material includes DNA isolated from tumor tissue, body fluids such as blood, serum, plasma, urine or faeces (see column 4, lines 17-25); (iii) the method is applicable to prognostic diagnosis of tumors and analysis of these loci was suitable (used) for making prognostic tumor diagnosis, tumor predisposition as well as detection of tumors of endometrium, the gastrointestinal tract and in particular colorectal tumors (see column 3, lines 42-45). However, Ruschoff et al. did not teach multiplex amplification and MONO-15 primers for amplification.

Schumm et al teach a multiplex amplification method to amplify short tandem repeat loci wherein Schumm et al. disclose that the method comprises co-amplification of at least three tandem repeat loci from one or more DNA samples and evaluating the amplified alleles in the mixture by comparing amplified alleles to a size standard (see column 4, lines 11-27 and column 6, lines 29-33). Further, Schumm et al. disclose that the method allows three or more, even as many as eight or more loci to be amplified in one tube using a single amplification reaction (see column 7, lines 61-67) and use of primers either labeled or unlabelled to evaluate the amplified alleles (see column 7, lines 36-60).

Kieback teach a method for diagnosing an increased risk for breast or ovarian cancer wherein Kieback discloses a primer sequence which comprises the instant MONO-15 primer, SEQ ID No. 8 (see SEQ ID No. 5, column 5, lines 11-12, and sequence alignment).

Sulston et al teach a sequence of homo sapiens BAC clone which comprises the instant MONO-15 primer, SEQ ID No. 7 (absolute match, see sequence alignment from GenEmbl database).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the method of analyzing micro-satellite instability as taught by Ruschoff et al. with the method of multiplex amplification as taught by Schumm et al., and primers as taught by Kieback and Sulston et al. because Ruschoff et al. states that 'it was determined that in different patients different classes of micro-satellites are affected with different frequencies of genomic instability, consequently an analysis of different classes of micro-satellite instability(MIN) is essential for a reliable determination of the RER phenotype with a limited number of PCR reactions' (see column 3, lines 1-5). One such alternative form of analysis to limit the PCR reactions expressly motivated by Schumm et al. is the use of multiplex amplification with different samples and multiple loci specific primers in one tube PCR reaction 'to provide a method for simultaneous amplification of multiple distinct polymorphic short tandem repeat loci using PCR or other amplification systems to determine, in one reaction, the alleles of each locus contained within the multiplex' (see column 3, lines 54-59). An ordinary practitioner would have been motivated to combine the method of Ruschoff et al. with the method of Schumm et al., Kieback and Sulston et al. in order to achieve the expected advantage of a rapid and sensitive method for detecting microsatellite instability.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 703-305-1004. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on 703-308-1152. The fax phone numbers for the

organization where this application or proceeding is assigned are 703-308-0294 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Suryaprabha Chunduru
November 21, 2001

JEFFREY FREDMAN
PRIMARY EXAMINER